REMARKS/ARGUMENTS

The Status of the Claims.

Claims 1-21 are pending with entry of this amendment, claims 22-23 being cancelled herein. Claims 1, 7 and 12 are amended herein. These amendments introduce no new matter and support is replete throughout the specification. These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter or agreement with any objection or rejection of record.

With respect to claim 1 and 7, support for the mixture of biospecific affinity reagents that specifically bind host cell proteins of a particular host organism can be found throughout the specification. For example, see specification at paragraphs [0032] to [0033] and [0071] through [0073]. Claim 12 has been amended to further clarify the invention with respect to antecedent basis.

Applicants submit that no new matter has been added to the application by way of the above Amendment. Accordingly, entry of the Amendment is respectfully requested.

The Election/Restriction Requirement.

Pursuant to a restriction requirement made final, Applicants cancel claims 22 and 23 with entry of this amendment. Please note, however, that Applicants reserve the right to file subsequent applications claiming the canceled subject matter and the claim cancellations should not be construed as abandonment or agreement with the Examiner's position in the Office Action.

The Information Disclosure Statement.

Applicants note with appreciation the Examiner's thorough consideration of the references cited in the Information Disclosure Statement (Form 1449) submitted on May 10, 2007.

35 U.S.C. §102.

Claims 1-6, 10-12, 15 and 19-21 were rejected under 35 U.S.C. §102(e) as allegedly anticipated by Monforte (USPN 7,091,046). Applicants traverse.

In order for a reference to anticipate an invention, the reference must teach each and every element of the claimed invention. Claims 1-6, 10-12, 15 and 19 are drawn to methods for determining the presence of host cell proteins in a sample, including the steps of (a) capturing host cell proteins from a sample onto a solid support comprising a mixture of biospecific affinity reagents that specifically bind host cell proteins of a particular host organism; and (b) detecting the captured host cell proteins. Claims 20 and 21 are drawn to methods of following purification of a target

protein including the steps of (a) profiling a sample comprising the target protein at one step of a purification process, wherein profiling comprises detecting the target protein in the sample and detecting host cell proteins in the sample using the method according to claim 1; (b) subjecting the target protein to at least one purification step; (c) profiling the sample comprising the target protein after the purification step, wherein profiling comprises detecting the target protein in the sample and detecting host cell proteins in the sample using the method according to claim 1; and, (d) comparing the relative amounts of the target protein and the host cell proteins in the sample detected by profiling..

Monforte is alleged to teach or describe multiplexed assays that employ a binding moiety, such as an antibody attached to a solid support. However, the cited publication does not teach all of the limitations of the claimed invention. For example, while Monforte employs antibodies as the "polypeptide binding components" displayed on the Monforte genetic package, the publication does not teach or disclose using a panel of host organism-specific affinity reagents. In addition, while Monforte discloses a binding moiety such as an antibody attached to a solid support at column 13, the subsequently-cited "polypeptide binding component" refer to by the Office and disclosed at column 17 in the Monforte publication is the second, phage-displayed binding moiety, and not an antibody attached to a substrate surface. Furthermore, while the claimed embodiment depicted in rejected claim 12 is drawn to methods in which the detecting step comprises washing unbound molecules from the resin and eluting captured host cell proteins from the resin, the Monforte passage cited by the Office (column 16, lines 25-45) actually teaches elution of the second antibody (part of a bacteriophage display vector), and not the captured target proteins ("Following a wash step to remove unbound components, the different bound bacteriophages (A, B, C) are eluted and used to infect a plurality of host cells.") Monforte does not teach detection of the captured host protein; rather, as noted at column 14, lines 1-8, "In the methods provided herein, the signal-generating element is a genetic package, such as a bacteriophage, that can infect and multiply within a host (the amplification component) and also code for the expression of a unique polypeptide (the detectable signal component) that is subsequently detected" (emphasis added).

Because the Office has not demonstrated that the cited art teaches every element of the claimed invention, Applicants submit that the rejection is improper and respectfully request that it be withdrawn.

35 U.S.C. §103(a).

CLAIMS 7-9 ARE PATENTABLE OVER MONFORTE AND HUTCHENS

Claims 7-9 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Monforte (USPN 7 091,046) in view of Hutchens et al. (US 2001/0014461). Applicants traverse.

Criteria for obviousness

Three requirements must be met for a *prima facie* case of obviousness. First, the prior art reference must teach all of the limitations of the claims. M.P.E.P § 2143.03. Second, there must be a motivation to modify the reference or combine the teachings to produce the claimed invention. M.P.E.P. § 2143.01. Third, a reasonable expectation of success is required. M.P.E.P. § 2143.02. The teaching or suggestion to combine and the expectation of success must be both found in the prior art and not based on Applicants' disclosure. M.P.E.P. §2143. Applicants submit that the claims are patentable over Monforte in view of Hutchens, because the cited publications do not meet these criteria.

The limitations of the claimed invention are not taught by the cited art

First, the cited publications, alone or in combination, do not teach all of the limitations of the claimed invention. Claims 7-9 are drawn to methods for determining the presence of host cell proteins in a sample, including the steps of (a) capturing host cell proteins from a sample onto a solid support comprising a mixture of biospecific affinity reagents that specifically bind host cell proteins of a particular host organism; and (b) detecting the captured host cell proteins, where the solid support comprises a SELDI biochip onto which the affinity reagents are immobilized.

Monforte is alleged to teach mulitplexed assays for determining protein levels within a sample. As helpfully stated by the Office, Monforte employs MALDI techniques but does not teach or describe SELDI biochips. Also, as noted above, Monforte also does not teach or disclose every element of the claimed invention, including using mixtures of affinity reagents that specifically bind host cell proteins from a particular host organism. Hutchens is alleged to disclose the advantages of SELDI techniques such as surface-enhanced neat desortpion (SEND) over MALDI. However, the teachings in Hutchens do not remedy the deficits in Monforte; Hutchens also does not teach or disclose using mixtures of host organism-specific affinity reagents. Since Monforte and Hutchens, alone or in combination, do not teach all of the limitations of the claimed invention, the first criterion for proving a *prima facie* case of obviousness has not been met.

There is no motivation provided to modify the Monforte and Hutchens methods

The Office has not provided a motivation to modify either the MALDI systems of Monforte or the SEDLI approach of Hutchens to produce the claimed invention, and thus has not met the second criterion for proving a *prima facie* case of obviousness.

Monforte provides an improved ELISA assay, having a first antibody coupled to a solid support (the affinity bead; see Figure 1); the first antibody captures the target protein, which then interacts with a member of a phage display library (second antibody) having a means for signaling (the marker component of the vector). It is the marker component, not the target molecule, that is then amplified and detected, e.g., by mass spectrometry (column 2, lines 40-52; column 14, lines 1-15; column 31, lines 28-39).

As helpfully noted by the Examiner, the Monforte publication states (column 17, lines 34-40) that "the polypeptide binding component includes an antibody or binding portion thereof." However, the referenced components are part of the Monforte "bio-displayed component" (i.e., phage display library), and as such are not coupled to a substrate surface as provided in the claimed invention. Monforte does not provide any motivation to either produce a phage display library using antibodies against host cell antigens of a particular host organism as the displayed ligands, or to couple such library members to the substrate surfaces employed in the Monforte methods.

Hutchens is alleged to teach the advantages of SELDI over MALDI techniques, but also does not provide any motivation to modify the Monforte display library members to produce affinity reagents against host cell proteins of a specified host organism, much less the claimed methods in which host cell proteins are captured using such reagents. Furthermore, there is no motivation to use a SELDI technique as described by Hutchens in the detection of the amplified markers of Monforte. In MALDI, the molecules being detected are mixed directly with the matrix, while in SELDI, the detected molecules are coupled to the substrate surface prior to addition of the matrix. Thus, an affinity reagent for the component to be detected (the Monforte marker component) is required for SELDI, but not necessary or employed in MALDI techniques. The Monforte publication notes that methods involve MALDI detection of the amplified marker component, not the substrate-bound target protein or the associated phage display library member, is one of numerous advantages of the Monforte methods over the standard detection methods of the time (see column 1, ine59 through column 2, line 36; and column 14, lines 9-15). There is no motivation provided in either publication to make the Monforte system more complicated by adding an additional affinity reagent for coupling the marker component to the MS probe (as necessitated in the SELDI technique),

or to otherwise attempt to detect the markers taught by Monforte to a SELDI-type system as disclosed in Hutchens.

The cited publications do not provide any motivation to produce a phage display library using antibodies against host cell antigens of a particular host organism as the displayed ligands, to couple such library members to the substrate surfaces employed in the Monforte methods, or to add a further affinity reagent for coupling the Monforte marker component to the MS probe (as necessitated in the Hutchens SELDI technique). Since there is no motivation to modify the references to produce the claimed invention (beyond that found in the specification of the subject invention), Applicants submit that the second criterion for proving a *prima facie* case of obviousness has not been met.

No reasonable expectation of success has been provided

Third, a reasonable expectation of success is required for proving a *prima facie* case of obviousness. Neither publication teaches or discloses mixtures of affinity reagents that specifically bind host cell proteins from a particular host organism. Absent such disclosure, one of skill in the art could not successfully produce the claimed methods in which the host cell proteins are captured onto a solid support having said mixture of biospecific affinity reagents that specifically bind host cell proteins of a particular host organism. Applicants respectfully submit that, since the cited publications, alone or in combination, do not provide a reasonable expectation of success, the third criterion for proving a *prima facie* case of obviousness has not been met.

Summary

Since Monforte and Hutchens, alone or in combination, do not meet the criteria for proving a *prima facie* case for obviousness (all of the claimed elements are not taught, there is no motivation to modify the cited art, nor is there a reasonable expectation of successfully producing the claimed invention given the provided teachings), Applicants submit that the claims are patentable over the cited art and respectfully request that the rejection be withdrawn.

CLAIMS 13 AND 14 ARE PATENTABLE OVER MONFORTE AND SCHWARTZ

Claims 13 and 14 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Monforte in view of Schwartz (2006 J. Mol. Recog. 9:672-674). Applicants traverse.

The rejected claims are drawn to methods for determining the presence of host cell proteins in a sample in which the solid support is a chromatographic resin derivatized with a capture molecule, such as Protein A, Protein G, or a mercaptoheterocyclic ligand, that binds the members of

the affinity reagent mixture. Monforte is alleged to teach or multiplexed assays for determining protein levels in a sample involving solid supports comprising a chromatographic resin. As helpfully noted by the Examiner, Monforte does not teach or describe derivatization of the support with a capture molecule such as mercaptoheterocyclic ligands, which teaching is allegedly found in Schwartz publication. However, neither publication teaches or describes methods involving a mixture of biospecific affinity reagents that specifically bind host cell proteins of a particular host organism. Furthermore, as noted above, the Monforte phage display library members are not coupled to the Monforte affinity bead and as such are not used to capture the target peptides onto the solid support as provided in the claimed invention. Neither publication provides either a motivation to modify the Monforte phage display library members, or an expectation of successfully producing the claimed methods given the teachings in the cited art.

Since Monforte and Schwartz, alone or in combination, do not meet the criteria for proving a *prima facie* case for obviousness (all of the claimed elements are not taught, there is no motivation to modify the cited art, nor is there a reasonable expectation of successfully producing the claimed invention given the provided teachings), Applicants submit that the claims are patentable over the cited art and respectfully request that the rejection be withdrawn.

CLAIM 16 IS PATENTABLE OVER MONFORTE AND PIASIO

Claim 16 was rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Monforte (USPN 7 091,046) in view of Piasio (USPN 4,098,876). Applicants traverse.

Claim 16 is drawn to methods in which the host cell proteins are first bound to the affinity reagent, and the affinity reagent is subsequently captured on the solid support. The Monforte methods allegedly involve "a binding moiety such as an antibody attached to a solid support captures the target protein and a second binding moiety comprising a second antibody with a signal-generating element that then binds to the captured target protein" (page 7 of the Office Action). The second antibody is the displayed element of a phage display vector; the phage vector also contains a marker component that is subsequently amplified and used for detection. As helpfully noted by the Examiner, Monforte does not teach or describe the step of first binding the target proteins to the "labeled antibody" (i.e., phage display library members having the detection means); such teaching is allegedly found in the Piasio publication. However, neither publication teaches or describes methods involving a mixture of biospecific affinity reagents that specifically bind host cell proteins of a particular host organism. Furthermore, as noted above, the "labeled" Monforte phage display library members are not coupled to the Monforte solid support, and as such are not capable of capturing the

target peptides onto the solid support as provided in the claimed invention. Neither publication provides either a motivation to modify the Monforte phage display library members, or an expectation that such modification would successfully produce the claimed methods.

Since Monforte and Piasio, alone or in combination, do not meet the criteria for proving a *prima facie* case for obviousness (all of the claimed elements are not taught, there is no motivation to modify the cited art, nor is there a reasonable expectation of successfully producing the claimed invention given the provided teachings), Applicants submit that the claims are patentable over the cited art and respectfully request that the rejection be withdrawn.

CLAIMS 17 AND 18 ARE PATENTABLE OVER MONFORTE, PIASIO, HUTCHENS AND SCHWARTZ

Claims 17-18 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Monforte (USPN 7 091,046) in view of Piasio in further view of Hutchens et al. (US 2001/0014461) and Schwartz (). Applicants traverse.

The rejected claims are drawn to methods in which the host cell proteins are bound to the affinity reagent and the affinity reagent is subsequently captured a SELDI biochip (solid support) derivatized with an affinity reagent-binding capture molecule, such as Protein A, Protein G, or a mercaptoheterocyclic ligand. Monforte is alleged to teach antibodies attached to chromatographic resins; however, Monforte does not teach SELDI biochips as solid supports, derivatization of said support with a capture molecule, or coupling of the target protein to the affinity reagent prior to capture upon the solid support. These deficits are allegedly remedied by Hutchens, Schwartz, and Piasio, respectively. However, none of the cited publications teach or describe methods involving a mixture of biospecific affinity reagents that specifically bind host cell proteins of a particular host organism. Furthermore, as detailed above, the Monforte phage display library members are not coupled to the Monforte affinity bead, and as such cannot be employed to capture the target peptides onto the solid support as provided in the claimed invention. Furthermore, none of the publications provide either a motivation to modify the Monforte phage display library members, or an expectation that such modification would successfully produce the claimed methods.

Since Monforte, Piasio, Hutchens and Schwartz, alone or in combination, do not meet the criteria for proving a *prima facie* case for obviousness (all of the claimed elements are not taught, there is no motivation to modify the cited art, nor is there a reasonable expectation of successfully producing the claimed invention given the provided teachings), Applicants submit that the claims are patentable over the cited art and respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the claims are deemed not to be in condition for allowance after consideration of this Response, a telephone interview with the Examiner is hereby requested (per the attached Applicant-Initiated Interview Request Form). Please telephone the undersigned at (510) 337-7871 to schedule an interview.

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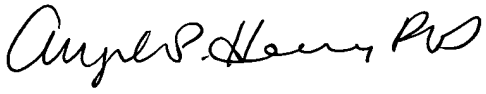
Respectfully submitted,



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Attachments:

1) A petition to extend the period of response for 1 month;
2) A transmittal sheet;
3) A fee transmittal sheet;
4) Applicant-Initiated Interview Request Form; and,
5) A receipt indication postcard.